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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/646,904	08/22/2003	Herbert Irschik	103832-510-NP	1332

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EXAMINER	
QAZI, SABIHA NAIM	
ART UNIT	**PAPER NUMBER**
1616	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/646,904	IRSCHIK ET AL.	
	Examiner	Art Unit	
	Sabiha Qazi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 September 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,9-14 and 18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 9-14 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Final Office Action

Claims 1–5, 9-14 and 18 are pending. No claim is allowed at this time. Amendments are entered.

Summary of this Office Action dated Saturday, November 25, 2006

1. Response to Remarks
2. Information Disclosure Statement
3. Copending Applications
4. Specification
5. 35 USC § 112 --- First Paragraph Written Description Rejection
6. 35 USC § 112 --- First Paragraph Scope of Enablement Rejection
7. 35 USC § 102(b) Rejections
8. Conclusion
9. Communication

Response to Remarks

- Rejection under 35 U.S.C. 112, second paragraph is withdrawn because claims are amended.
- All other rejections are maintained because arguments are not found persuasive. The proviso in claim 1 is considered "new matter". The negative limitation as amended does not have support in the disclosure. Applicant is kindly requested to tell the office the support of excluded subject matter.
- The response is silent about the support of new claim 18. Applicant is again kindly requested to tell the office about the support of claim 18. The diseases as listed were not in the disclosure.
- Applicant argues that the reference does not anticipated claim 3, which is composition claim. Examiner respectfully disagrees because the compositions claims are included in the rejection, when the compound is anticipated its composition is also anticipated. Composition is not separated from compounds.
- In order to advance the prosecution Applicant may consider calling the Examiner to discuss the issues surrounding this application.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information

submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

Copending Applications

Applicants must bring to the attention of the examiner, or other Office official involved with the examination of a particular application, information within their knowledge as to other copending United States applications, which are "material to patentability" of the application in question. MPEP 2001.06(b). See Dayco Products Inc. v. Total Containment Inc., 66 USPQ2d 1801 (CA FC 2003).

Specification

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

35 USC § 112 --- First Paragraph Written Description Rejection

1. Claims 1–5, 9-14 and 18 rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The disclaimed invention finds no support in the original disclosure.

The rejection is based on the proviso in claim1, which is not supported by an adequate written description in the original disclosure. MPEP 2173.05(i) states: "Any negative limitation or exclusionary proviso must have basis in the original disclosure. See In re Johnson, 558 F.2d 1008, 1019, 194 USPQ 187, 196 (CCPA 1977). In *In re Johnson*, the court noted that any negative limitation or exclusionary proviso *must have basis in the original disclosure. Only* if alternative elements are positively recited in the specification, they may be explicitly excluded in the claims. In the present case the negative limitation/exclusionary proviso does not have basis in the original disclosure, and the alternative elements were not positively recited in the specification, they are generically disclosed, so the Appellants' argument is not relevant to the current issues.

In the present case compounds were generically disclosed and claimed (claim 1). After the rejection Applicants have disclaimed the compounds, which were anticipated and/or obvious.

See also Ex parte Grasselli, 231 USPQ 393 (Bd. App. 1983), aff'd mem., 738 F.2d 453 (Fed. Cir. 1984). Any claim containing a negative limitation, which does not have basis in the original disclosure, should be rejected under 35 U.S.C. 112, first paragraph as failing to comply with the written description requirement.

The instant claims therefore are rejected under 35 U.S.C. 112, first paragraph, under instruction from MPEP 2173.05(i), because they contain a negative limitation that does not have basis in the original disclosure.

In *Purdue Pharma LP v Faulding, Inc., 230 F.3d 1320, 1326, 56 USPQ2d 1481, 1486 (Fed. Cir. 2000)*, the court noted that with respect to *In re Ruschig, 371 F.2d 990, 154 USPQ 118 (CCPA 1967)*,

"Ruschig makes clear that one cannot disclose a forest in the original application, and then later pick out a tree of the forest and say, "here is my invention". In order to satisfy the written description requirement, the blaze marks directing the skilled artisan to that tree must be in the originally filed disclosure."

Purdue is relevant in this case, because the Applicants disclosed a genus ("a forest") in the original application, then later picked out some specific compounds ("a tree of the forest"), and are now saying, "here is my invention". In order to satisfy the written description requirement, according to *Purdue*, the Applicants must disclose the specific compounds in the originally filed disclosure." (See (56 USPQ2D 1481).

More from *Purdue*: The case of In re Ruschig, 379 F.2d 990, 154 USPQ 118 (CCPA 1967), is instructive here (see page 1487). The claim at issue in that case was directed to a single compound. The appellants argued that, although the compound itself was not disclosed, one skilled in the art would find support for the claimed compound in the general disclosure of the genus of compounds to which the claimed compound belonged. The Ruschig court rejected that argument, stating: [i]t is an old custom in the woods to mark trails by making blaze marks on the trees. It is of no help in finding a trail or in finding one's way through the woods where the trails

have disappeared-or have not yet been made, which is more like the case here-to be confronted simply by a large number of unmarked trees. We are looking for blaze marks, which single out particular trees. We see none. *Id.* at 994-95, 154 USPQ at 122.

35 USC § 112 --- First Paragraph Scope of Enablement Rejection

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> *The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.*

Claims 1–5, 9-14 and 18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for certain method of treatments does not reasonably provide enablement for all the method of use such as treatment of oncoses (claim 4) , uncontrolled proliferation of endogenous cells (claim 5), infective diseases, immunomodulatory action as claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of

the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

The nature of the invention

Presently claimed invention is drawn to a disorazole derivative as in claim 1, composition and their method of use.

The predictability or unpredictability of the art

There is a lack of predictability in the art. Table 1 on page 16 discloses the inhibition of proliferation by Disorazole E1, D1 and A1 according to the invention in the XTT cytotoxicity test on human cell lines (proliferation assay, EC50 in □g/ml). Tables 2-4 and comparison with the reference compounds has been fully considered. There is no example to use the compound with another "antitumor agent" or signal transduction inhibitors".

New claim 18 is drawn to various tumor diseases and a long list of tumor diseases are claimed. The compounds

There is lack of predictability in the in the pharmaceutical art especially in the methods for treatment of cancer.

Evidence involving a single compound and two types of cancer was not found sufficient to establish the enablement of claims directed to a method of treating rapid and uncontrolled

proliferation of endogenous cells comprising adimistering the compound of Formula 1a as in claim 5.

See In re Buting, 163 USPQ 689. The disclosure provides no indication of whether the compounds treat all cancers. To make clearer the lack of enablement for treatment of all cancer, extrinsic evidence is supplied by Draetta (Ann. Reports Med. Chem.), Draetta et al. in "Annual Reports in Medicinal Chemistry"., 1996, Academic Press, San Diego, pp 241-246, final sentence on page 246 although many still think about the need for a magic bullet as a cure for all cancers, our knowledge of the molecular mechanism underlying this disease make the prospect of developing such a universal cure very unlikely." Since no universal cure for cancer has been developed, it follows that there is no correlation between the assays relied upon by applicants and the ability to treat all types of diseases base on rapid and uncontrolled proliferation of endogenous cells. Thus, the data as presented are not sufficient to enable such claims.

Further, in the art of clinical oncology, no compound has yet shown clinical efficacy against every type of cancer. Different agents are used for different forms of cancer and no single agent is listed as a treatment of every single type of cancer. Balasubramanian reference (Recent Developments in Cancer Cytotoxics) on page 151 first paragraph "the successful treatment of solid tumors remains a formidable challenge."

Applicant has provided no evidence, which incontrovertibly demonstrates that the tests set forth in the instant specification are art-recognized, reliable predictors of successful treatable, in vivo, of all cancers by all the compounds as claimed. The worker of ordinary skill in the art would not be able to practice the instantly claimed method, since no description is found of an actual method wherein a cancer in a host is treated.

There is no teaching as to how the claimed compound(s) for the "treatment of a disease in humans or animals which is based on rapid and uncontrolled proliferation of endogeneous cells comprising administering the compound of claim 1 to a human or animal in need of such a treatment". (claim 5). The treatment of oncoses, uncontrolled proliferation, sarcoma, acute lymphatic leukemia (ALL) acute promyleotic leukemia (APL) Hodgkin's disease, lung carcinoma and many more by disorazole compounds of formula I as in claim 1 is not predictable. The specification provides test data for proliferation of three disorazole compounds A1, D1 and E1,

The "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art.

On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Accordingly, what is known in the art provides evidence as to the question of predictability. In particular, the court in *In re Marzocchi*, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971), stated:

[I]n the field of chemistry generally, there may be times when the well-known unpredictability of chemical reactions will alone be enough to create a reasonable doubt as to the accuracy of a particular broad statement put forward as enabling support for a claim. This will

especially be the case where the statement is, on its face, contrary to generally accepted scientific principles. Most often, additional factors, such as the teachings in pertinent references, will be available to substantiate any doubts that the asserted scope of objective enablement is in fact commensurate with the scope of protection sought and to support any demands based thereon for proof.

The scope of the required enablement varies inversely with the degree of predictability involved, but even in unpredictable arts, a disclosure of every operable species is not required. A single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements.

See *In re Vickers*, 141 F.2d 522, 526-27, 61 USPQ 122, 127 (CCPA 1944); *In re Cook*, 439 F.2d 730, 734, 169 USPQ 298, 301 (CCPA 1971). However, in applications directed to inventions in arts where the results are unpredictable, the disclosure of a single species usually does not provide an adequate basis to support generic claims. *In re Soll*, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938).

In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work. See MPEP 2164.03.

The amount of direction or guidance presented

The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification.

In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling. See, e.g., *Chiron Corp. v. Genentech Inc.*, 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004) ("Nascent technology, however, must be enabled with a 'specific and useful teaching.'

The law requires an enabling disclosure for nascent technology because a person of ordinary skill in the art has little or no knowledge independent from the patentee's instruction. Thus, the public's end of the bargain struck by the patent system is a full enabling disclosure of the claimed technology."

The presence or absence of working examples

A disclosure should contain representative examples, which provide reasonable assurance to one skilled in the art that the compounds fall within the scope of a claim will possess the

alleged activity. See In re Riat et al. (CCPA 1964) 327 F2d 685, 140 USPQ 471; In re Barr et al. (CCPA 1971) 444 F 2d 349, 151 USPQ 724.

The quantity of experimentation necessary

Since there is no guidance and/or direction provided by the Applicants for method of treatment of oncoses, uncontrolled proliferation, sarcoma, acute lymphatic leukemia (ALL) acute promyleotic leukemia (APL) Hodgkin's disease, lung carcinoma and many more by disorazole compounds of formula I as in claim 1 one skilled in the art would have to go through undue experimentation to make and/or use the instant invention.

The specification provides test data for proliferation of three disorazole compounds A1, D1 and E1, the claims are too broad and disclosure does not provide guidance or direction for the treatment of all the diseases as claimed.

The first paragraph of 35 USC 112 requires "*...such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains...*" The instant invention fails to meet this requirement, as it lacks such full, clear, and concise manner as to enable any person skilled in the art to which it pertains to make and/or use the invention.

Applicants fail to fulfill the requirement of 35 U.S.C. 112, first paragraph, by failing to provide an adequate written description of how to treat all cancers in a single host.

35 USC § 102(b) Rejection—1st Rejection

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by JANSEN et al. (Liebig Ann. Chem. (1994), 759-773). See disarozole compound 19-21 on page 765, same compounds has been claimed in present invention.

35 USC § 102(b) Rejection—2nd Rejection

Claims 1-4 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by IRSCHIK et al., (The J. of Antibiotics). See Fig. 1 and Table 1 on page 31.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after

the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Communication

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Qazi, Ph.D. whose telephone number is 571-272-0622. The examiner can normally be reached on any business day.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Johann Richter, Ph.D. can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

S. Qazi

SABIHA QAZI, PH.D
PRIMARY EXAMINER